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PHASE 3 SUMMARY OF MRID 00094004:

ACUTE DERMAL TOXICITY IN THE RABBIT

STUDY # 2338-81

PRIME+ (FLUMETRALIN)

GUIDELINE REFERENCE:

81-2 ACUTE DERMAL TOXICITY IN THE RABBIT

SUMMARY PREPARED BY:

JACQUELINE GILLIS, Ph.D.

MERRILL TISDEL

14 SEPTEMBER 1990

ORIGINAL STUDY PREPARED BY:

STILLMEADOW, INC.

HOUSTON, TEXAS

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C).

Company: CIBA-GEIGY Corporation (Typed Name)

Company Agent: Thomas Parshley (Typed Name)

Title: Senior Reg. Specialist

Signature: _____ Date: _____

These data are the property of the Agricultural Division of CIBA-GEIGY Corporation, and as such, are considered to be confidential for all purposes other than compliance with FIFRA §10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality which may exist under any other statute or in any other country.

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STILLMEADOW, Inc. GLP Compliance Statement

This study was designed and performed in STILLMEADOW, Inc.'s AAALAC accredited laboratory in conformance with Good Laboratory Practice Standards for Nonclinical Laboratory Studies as specified by Department of Health, Education, and Welfare Food and Drug Administration (FR 59986, Dec. 22, 1978).

Robert J. Saboi
STILLMEADOW, Inc.

This study does not meet the requirements for 40 CFR Part 160 since it was conducted prior to the issuance of the EPA Good Laboratory Practice Standards. It was conducted according to the FDA Good Laboratory Practice Standards as indicated above.

Submitter/Sponsor of Study:

Merrill Tisdel
Agricultural Division
CIBA-GEIGY Corporation
Greensboro, North Carolina

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Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative:

Signature/Date: Merrill Tisdel 10.15.90

Typed Name: Merrill Tisdel

Title: Toxicologist

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.

Submitter's Representative:

Signature/Date: Merrill Tisdel 10.15.90

Typed Name: Merrill Tisdel

Title: Toxicologist

R406MT0628MG

81-2 Acute Dermal Toxicity in the Rat, Rabbit or Guinea Pig

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. N Technical form of the active ingredient tested. (for reregistration only)
2.* Y At least 5 animals/sex/group
3.* Y Rats 200-300 gm, rabbits 2.0-3.0 kg or guinea pigs 350-450 gm.
4. Y Dosing, single dermal.
5. Y Dosing duration at least 24 hours.
6.* NA Vehicle control, only if toxicity of vehicle is unknown.
7. Y Doses tested, sufficient to determine a toxicity category or a limit dose (2000 mg/kg).
8. Y Application site clipped or shaved at least 24 hours before dosing
9. Y Application site at least 10% of body surface area.
10. N Application site covered with a porous nonirritating cover to retain test material and to prevent ingestion.
11. Y Individual observations at least once a day.
12. Y Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
13. Y Individual daily observations.
14.* Y Individual body weights.
15.* Y Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

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IDENTIFICATION OF TEST MATERIAL

Chemical Name

CAS Name: N-(2-Chloro-6-fluorobenzyl)-N-ethyl-α,α,α,-trifluoro-2,6-dinitro-p-toluidine

or

2-Chloro-N-[2,6-dinitro-4-(trifluoromethyl)phenyl]-N-ethyl-6-fluorobenzenemethanamine

Common Name: Flumetralin

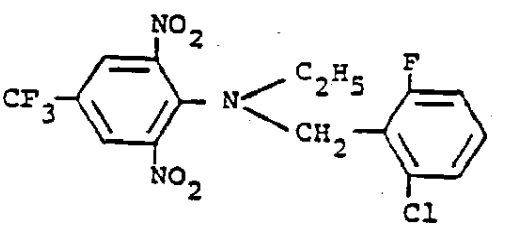
Trade Name: Prime +®

CIBA-GEIGY Code Number: CGA-41065

CAS Registry Number: 62924-70-3

EPA Shaughnessy Number: Unknown

Chemical Structure:



Percent Active Ingredient

Prime +®: 15.0% (Inert, 85.0%)

Identity and Composition of Impurities

Not required for formulated product

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Prime+: 81-2: Acute Dermal Toxicity in the Rabbit

1. The test article was Prime+ (CGA-41065 15E), a clear orange liquid, FL-810737.

2. Five male and five female New Zealand white rabbits were tested at one dose level (a limit dose).

3. Male animals weighed between 2.3 and 2.8 kg and female animals weighed between 2.3 and 2.7 kg when tested.

4. The test article was applied to the exposure area on the back of the trunk of each animal one time.

5. The duration of dermal exposure was 24 hours.

6. No vehicle was used for application of the test article; therefore, a vehicle control was not necessary.

7. Dose tested and results were:

Dose (mg/kg)	Number Dead/Number Treated		
	Males	Females	Overall
2010	1/5	0/5	1/10
LD_{50} (mg/kg)	>2010	>2010	>2010

8. The animals were prepared approximately 24 hours prior to treatment by clipping a portion of the back of the trunk of each animal free of hair. Immediately prior to application of the test article, two longitudinal and two perpendicular epidermal abrasions were made on each exposure area with the point of a hypodermic needle. The abrasions penetrated the stratum corneum but did not disturb the derma or cause bleeding.

9. The area of the application site was approximately 30% of the total body surface.

10. Following application of the test material, the application site was covered with a layer of polyethylene which was held in place with masking tape.

11. Observations for pharmacologic and/or toxicologic effects and mortality were recorded at 0.5, 3, and 6 hours after dosing. None of the animals exhibited toxicologic effects on the day of dosing.

12. Individual observations were made at least once daily for 14 days after the day of dosing. All female animals appeared normal for the duration of the study. One male animal died on Day 9, with no prior abnormal observations. Signs of mucoid diarrhea, no or few feces, difficulty breathing, and activity decrease were observed in at least one male animal; all surviving animals appeared normal by Day 14.

13. See Items 11 and 12.

14.

Dose	Body Weights (kg) (Mean/Number Alive)					
	Males			Females		
(mg/kg)	Initial	Day 7	Day 14	Initial	Day 7	Day 14
2010	2.51/5	2.51/5	2.73/4	2.50/5	2.68/5	2.86/5

15. A gross necropsy examination was conducted on the animal which died during the study and all surviving animals at study termination. Findings of yellow mucoid material in the small intestine were observed in the animal which died. No other treatment-related abnormalities were observed.

16. There were no significant changes from the Acceptance Criteria in this study. One deviation from the Acceptance Criteria is noted. Under Item 10, the application site was covered with an occlusive covering rather than a porous covering. This deviation is considered to be insignificant because, in general, the procedure used would tend to enhance absorption and increase whatever toxic effects might develop; even with this possibility of heightened effects, the LD_{50} was >2010 mg/kg. It is also noted that the test article was the formulated product rather than the technical material. The report of an acute dermal toxicity study with the technical material (MRID 00093999) is also summarized in this Phase 3 submission.

GILLIS:R510SW0921JG/MT